Subpart F—Dermatologic Dosage Forms

Subparts G–I—[Reserved]

Subpart J—Certain Other Dosage Forms

AUTHORITY: Sec. 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357).

SOURCE: 39 FR 19046, May 30, 1974, unless otherwise noted.

Subpart A—Bulk Drugs

§ 444.6 Amikacin.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Amikacin is A-3-amino-3-deoxy-A-D-glucopyranosyl (1–6) - A - [6 - amino - 6 - deoxy - A - D - glucopyranosyl (1–4)] - N^1 - [(*s*) - 4 - amino - 2 - hydroxy - 1 - oxobutyl] - 2 - deoxy - D - streptamine. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its moisture content is not more than 8.5 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 9.5 and not more than 11.5.

(v) It gives a positive identity test for amikacin.

(vi) Its residue on ignition is not more than 1.0 percent.

(vii) Its specific rotation is not less than +97° and not more than +105°.

(viii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, safety, moisture, pH, identity, residue on ignition, specific rotation, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of

this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient sterile distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 10.0 micrograms of amikacin per milliliter (estimated).

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Identity.* Proceed as directed in § 436.318 of this chapter.

(6) *Residue on ignition.* Proceed as directed in § 436.207(a) of this chapter.

(7) *Specific rotation.* Proceed as directed in § 436.210 of this chapter, using an aqueous solution containing 20 milligrams of amikacin per milliliter and a 1.0-decimeter polarimeter tube. Calculate the specific rotation on an anhydrous basis.

(8) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[41 FR 49483, Nov. 9, 1976, as amended at 44 FR 10379, Feb. 20, 1979; 50 FR 19919, May 13, 1985]

§ 444.7 Amikacin sulfate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Amikacin sulfate is the sulfate salt of *D*-streptamine, *0*-3-amino-3-deoxy-α-*D*-glucopyranosyl(1-6)-*0*-[6-amino-6-deoxy-α-*D*-glucopyranosyl(1-4)]-N^1-(4-amino-2-hydroxy-1-oxobutyl)-2-deoxy-,(S)-. It is so purified and dried that:

(i) Its potency is not less than 674 micrograms and not more than 786 micrograms per milligram on an anhydrous basis if the molar ratio of amikacin to sulfuric acid (H_2SO_4) is 1:2 and is not less than 691 micrograms and not more than 806 micrograms per milligram on an anhydrous basis if the molar ratio of amikacin to H_2SO_4 is 1:1.8.

(ii) Its loss on drying is not more than 13.0 percent.

(iii) The pH of an aqueous solution containing 10 milligrams of amikacin sulfate per milliliter is not less than 2.0 and not more than 4.0 if the molar ratio of amikacin to H_2SO_4 is 1:2 and not less than 6.0 and not more than 7.3 if the molar ratio of amikacin to H_2SO_4 is 1:1.8.

(iv) It gives a positive identify test for amikacin.

(v) Its residue on ignition is not more than 1.0 percent.

(vi) Its specific rotation is not less than +76° and not more than +84° on the anhydrous basis.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, pH, identity, residue on ignition, specific rotation, and crystallinity.

(ii) Samples, if required by the Center for Drug Evaluation and Research: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.216 of this chapter, using a 25-centimeter by 4.6-millimeter column packed with irregular 5-micron octadecyl hydrocarbon bonded silica, thermostatted at 30 °C, an ultraviolet detection system operating at a wavelength of 340 nanometers, a flow rate not exceeding 2.0 milliliters per minute, a chart speed of 1.0 centimeter per minute (the chart speed is increased to 5.0 centimeters per minute to obtain chromatograms used for performance parameter determinations), and a known injection volume between 15.0 and 30.0 microliters. Retention times of amikacin and kanamycin are about 10 and 15 minutes, respectively. Reagents, working standard solution, sample solution, resolution test solution, system suitability requirements, and calculations are as follows:

(i) *Reagents*—(A) *1.0 percent 2,4,6-trinitrobenzenesulphonic acid solution.* Dissolve 1.0 gram of 2,4,6-trinitrobenzenesulphonic acid in 100 milliliters of distilled water.

(B) *0.02M potassium dihydrogen phosphate.* Dissolve 2.72 grams of potassium dihydrogen phosphate in 800 milliliters